



Benefits Collaborative FAQs: Genetic Testing

This FAQ document summarizes:

- Frequently asked questions regarding Colorado Department of Health Care Policy and Financing (Department) efforts to develop a genetic testing policy through the Benefits Collaborative Process; and
- Suggestions made within the Benefits Collaborative Process, and supported by more than one stakeholder, for how to improve the draft Genetic Testing Benefit Coverage Standard.

Below each item, the Department has provided an *interim* response.

Important Note: The development of a Genetic Testing Benefit Coverage Standard is ongoing; there are many stages of the Benefits Collaborative Process that the draft has yet to complete. This FAQ document is a snap-shot of the Department position as of 9/29/2015 and should not be read as a final policy determination

Item 1

What *was* the genetic testing policy proposed by the Department as of February 12, 2015?

- On February 12, 2015, the Department proposed that gene variants may be tested, and/or specific genetic tests may be performed, for adults 21 and older, when certain client indications are present, as listed in the "Tier 1" or "Green" criteria established by the Centers for Disease Control (CDC) Office of Public Health Genomics.
 - The CDC ranks a list of testable gene *variants* – and, in some cases, calls-out specific *tests* – according to:
 - The level of evidence that exists to support the clinical utility of genetic testing when certain client *indications* are present; and/or
 - The level of evidence that exists to support the clinical utility of genetic testing when a specific *family health history* is present.
 - These gene *variant/test/indication/family history* groupings are ranked into three tiers: Tier 1 (Green); Tier 2 (Yellow); and Tier 3 (Red).



- Example from CDC Tier 1: Robust evidence of clinical utility exists to support testing for Lynch Syndrome (*variant/test*) when someone is newly diagnosed with colorectal cancer (*indication*) for the purpose of screening.
- Another Example from CDC Tier 1: Robust evidence of clinical utility exists to support testing for Lynch Syndrome (*variant/test*) when there is an established *family history* of Lynch Syndrome for the purpose of diagnosis and screening.
- Those *variant/test/indication/family history* groupings that appear in CDC Tier 1 are supported by the greatest body of evidenced based research, *in addition* to meeting one or more of the following three criteria:
 - FDA label requires use of test to inform choice or dose of a drug (applies only to pharmacogenetic tests)
 - CMS covers testing
 - Clinical practice guidelines based on systematic review support testing

Item 2

Why is the Department proposing that the CDC Guidelines be used to determine which genetic tests are covered under Colorado Medicaid?

- The CDC uses a rigorous methodology, which includes a peer reviewed process, established in the medical literature. It provides the Department with an unbiased list of conditions under which a test should be covered.
- *Variant/indication/family history* combinations that warrant specific testing are assessed for both statistical and clinical validity, as well as the benefit to the client.
- The CDC Tiers are easy-to-follow guidelines which are reviewed frequently and will expand with scientific breakthroughs in this rapidly changing field.
- Using national criteria allows the Department to provide medically necessary genetic testing, without delaying client care in order to conduct research.
- **IMPORTANT NOTE:** As of June 30, 2015, the Department proposes to expand coverage to *certain* tests that *do not* presently meet the criteria established on CDC Tier 1 (see Items 6 and 10 below for further details). In addition to covering a select group of tests not on CDC Tier 1, the Department will continue to cover *all* tests that meet the criteria established on CDC Tier 1, for the reasons listed above.



Item 3

How can I learn more about the Department's proposal?

- To learn more about what the Department proposed at the start of the 2015 Genetic Testing Benefits Collaborative Process – and why, you may view the Power Point presentation dated February 12th, 2015, located on the Benefits Collaborative Meeting Schedule webpage at <https://www.colorado.gov/pacific/sites/default/files/Benefits%20Collaborative%20Genetic%20Testing%20Presentation%20February%2012%2C%202015.pdf>
- The revised, draft Genetic Testing Benefit Coverage Standard, which includes changes to proposed policy made *after* February 12th, 2015 may be found at the following link: <https://www.colorado.gov/pacific/sites/default/files/Benefits%20Collaborative%20Genetic%20Testing%20Draft%20Standard%20Revised%20July%202015%20February%2012%2C%202015.pdf>

Item 4

How should a provider interpret the criteria (groupings) on CDC Tier 1?

Is the existence of a particular indication or family history and the desire to test for an associated gene variant – as listed in CDC Tier 1 – enough to warrant testing, or do all three of the additional CDC Tier 1 criteria mentioned above (in Item 1, on page 2) also need to be met in order for a test to be covered?

- The existence of a particular indication or family history, and the desire to test for an associated gene variant - as listed in CDC Tier 1 - would be enough to warrant testing.
- The three criteria mentioned above are criteria the CDC used to *create* Tier 1.

Since, in many cases, CDC Tier 1 details specific *variant/indication* groupings, how will providers know which genetic *test(s)* is covered?

- All practitioners able to counsel a client regarding genetic testing should have the knowledge and tools necessary to identify the appropriate test to be ordered.
 - A full list of billable procedure codes will be accessible in the Provider Fee Schedule on the Department website at: <https://cohcpf.sharepoint.com/sites/HPO/HPBO/Ops/BC/colorad.gov/hcp>
 - The proposed Genetic Testing Benefit Coverage Standard is clear that "If a Practitioner is unable to counsel a client regarding genetic testing, they must refer the client to a provider capable of providing genetic counseling prior to ordering the test."



Item 5

What is the CDC's process for developing and updating Tier 1, 2 and 3?

How are the CDC tiers developed?

- **IMPORTANT NOTE:** The field of genetic testing is rapidly expanding, and therefore there is often insufficient high quality evidence supporting the use of genetic testing. The CDC criteria for ranking genetic testing by levels of evidence provides a useful starting place for determining appropriate coverage of genetic testing.
 - The Department has invited stakeholders to provide additional research and suggestions and, subsequent to the stakeholder meeting on February 12, 2015, has *broadened* genetic testing coverage described in the proposed coverage standard to include certain tests that *do not* meet the criteria listed on CDC Tier 1, as detailed below.
- The CDC uses the tier system to more easily see and stratify what different evaluation groups have said, in general, about particular tests.
 - Per CDC staff, the CDC devised and tried out different approaches to categorizing, and came to an agreement that the schema presented was useful to them, and hopefully others, as a means of getting a broad picture of the distribution of evidence in the field.
 - Further information on how the CDC tier system and criteria was developed is contained in the CDC Clinical Pharmacology and Therapeutics article found at the following link: <http://www.ncbi.nlm.nih.gov/pubmed/24398597>

How often is the list reviewed?

- Per CDC staff, a horizon scan is conducted weekly to identify new research and guidelines which may require a revision to the CDC Tiers.
- The Department will review both the CDC list, and any and all additional policy criteria placed in the coverage standard, on an annual basis and will amend Colorado Medicaid policy as needed.

How might stakeholders engage with CDC regarding the development of this list?

- The CDC Office of Genomics uses the list to represent a broad picture of the distribution of evidence in the field.
- Per CDC staff, there is no formal public engagement process when stakeholders wish something to be added to the list, but the CDC is open to anyone contacting them to let them know of key sources that may be missing from the list (e.g., a guideline or systematic review).
- **IMPORTANT NOTE:** Colorado has appropriated CDC Tier criteria for the purpose of ensuring that covered genetic tests have a *basis* of evidence. As such, recommendations for other genetic tests that should be covered under Colorado Medicaid should continue to be addressed to the Colorado Department of Health Care Policy and Financing (not the CDC Office of Genomics) for review and inclusion in the Genetic Testing Benefit Coverage Standard.



Item 6

Why are the *variant/test/indication/family history* groupings listed in Tier 2 of the CDC guidelines not covered?

- The Department has reviewed the information provided to us by stakeholders after February 12, 2015 and has also engaged the Medicaid Evidence Based Decisions Program (part of Oregon Health Science University) to review - for clinical utility - additional coverage suggestions made by stakeholders.
- As a result of this review, the Department has determined that genetic testing coverage should extend to certain additional tests, including several tests indicated by the *variant/indication/family history* groupings on the CDC Tier 2 list. The circumstances under which additional tests on CDC Tier 2 may be covered will be listed individually within the Genetic Testing Benefit Coverage Standard and are also listed below.
- As of July 29, 2015, the Department proposes that the following additional criteria, when met, allow for genetic testing:
 - Testing ER-alpha and PgR status/ER-alpha (ESR1) modulating agents for the purpose of risk prediction and prognosis when the following indications are present:
 - Ductal carcinoma in situ
 - Invasive breast cancer
 - Testing for Lynch syndrome when:
 - Patients meet revised Bethesda guidelines or Amsterdam criteria; or
 - Show a 5% or higher risk of Lynch syndrome based on any established prediction model; or
 - There is a MSI - H histology in colorectal cancer in patients younger than 60 years; or
 - Colorectal cancer has been diagnosed in patients:
 - With relatives (two or more first- or second-degree) with Lynch syndrome related cancer at any age; or
 - With relatives (one or more first-degree) with Lynch syndrome related cancer that was diagnosed under age 50 years; or
 - Under 70 years of age
 - Over 70, when Bethesda guidelines are met
 - Testing for the following mutations for the purpose of risk prediction and prognosis when Acute myeloid leukemia is indicated:
 - FLT3-ITD
 - CEBPA mutation
 - NPM1 mutation
 - KIT mutation



There are diagnostic genetic tests, such as those that identify hereditary cancers, which appear in CDC Tier 2 and for which there is a body of evidence demonstrating clinical utility. These tests should be covered.

- As of July 29, 2015 the Department proposes expanding genetic testing coverage to include several hereditary cancers which appear on CDC Tier 2, as specified immediately above.

Pediatric medical genetic tests are not listed in CDC Tier 1; they first appear in CDC Tier 2. It is important that children receive medically appropriate genetic tests.

- Limitations (on the types of *variant/indication/family history* groupings that may be tested), specified in the coverage standard, do not apply to children. Federal Early Periodic Screening, Diagnostic, and Treatment (EPSDT) guidelines stipulate that the medical needs of children age 20 years and younger must be evaluated on a case-by-case basis and that services determined to be medically necessary must be covered whether or not such services are covered under the State Plan.
- Language explaining the EPSDT exception has been added to the coverage standard.

Item 7

There are potential problems with the CDC Guidelines that the Department should address

The CDC tiers are based on markers and single genetic variants that do not allow for testing of a combination of genes.

- The field of genetic testing is rapidly expanding; the Department plans to re-assess genetic testing policy annually. The Department will re-evaluate non-coverage of combination gene testing in the future, as a larger body of evidence of clinical utility becomes available. However, at this time, the level of evidence is not sufficient to support coverage of a particular genetic panel or assay.
- Certain tier categorizations, if used to approve or deny coverage of a test, lead to puzzling outcomes. For example, a 50 year old newly diagnosed with hereditary colorectal cancer may not be tested for Lynch syndrome per Tier 2 criteria, but an 80 year old newly diagnosed with colorectal cancer may be tested, per Tier 1 criteria.
- As of July 29, 2015 the Department proposes expanding testing for Lynch syndrome to include 50 year olds who are newly diagnosed with hereditary colorectal cancer (see Item 6 above).



Item 8

Can the Department consider basing its policy on an alternative list of national, evidence-based guidelines, or supplementing the CDC tier criteria with criteria from another set of guidelines?

- The Department previously considered using ACCE criteria and a clinical decision making tool to determine coverage, however, stakeholder feedback was clear that the model was not workable.
- Other national guidelines lack sufficient evidence of clinical utility for all recommended tests, or clear explanation of the methodologies used to arrive at certain determinations.
- The Department is able to adopt coverage of groupings on CDC Tier 1, in part, because the list is discrete and because the level of evidence is clear.
- Where the Department has determined that sufficient evidence exists for the clinical utility and cost effectiveness of certain *variant/indication/family history* groupings *not* found on CDC Tier 1, the Department has expanded coverage within the draft coverage standard to include those associated tests.

Medicare uses Palmetto GBA MoDX Technical Assessment guidelines, which are more expansive. These guidelines allow for coverage of tests that have proven analytical and clinical validity as well as clinical utility.

- The Department seeks to ensure that covered tests are clinically util. Many tests on the MoDX list do not possess demonstrated clinical utility.
- The field of genetic testing is rapidly expanding; the Department plans to re-assess genetic testing policy annually, as more evidence becomes available.

National Comprehensive Cancer Network (NCCN) guidelines are also more expansive. These guidelines are used by clinical practitioners, are evidence based and are reviewed regularly. They include coverage of many hereditary tests not currently found in the CDC list.

- While NCCN guidelines are an important resource for background to any oncology topic, the methodology used by NCCN to establish certain guidelines lacks transparency on important development points.
- Many of the NCCN's recommendations, as stated on the NCCN website, are based on "low quality evidence" and panel review. While these recommendations may be important for physician/patient conversations, they are insufficient to support Medicaid Coverage.



Item 9

On February 17, 2015, Assurex Health provided the Department with a clinical dossier, four peer reviewed publications and a Medicare Local Coverage Determination, supporting coverage of the GeneSight Psychotropic assay, the purpose of which is to help clinicians determine the right medication for individual patients suffering from neuropsychiatric disorders.

- At this time, the Department will not cover the GeneSight Psychotropic assay. Some of the factors that have informed the Department decision *not* to cover testing at this time, are as follows:
 - Patient characteristics are minimally described in the studies provided, making it difficult to draw conclusions about the assays applicability to the Medicaid population.
 - The combination of Randomized Control Trials (RCT) and observational studies in the meta-analysis, as described within the dossier provided, is not common practice.
 - Only one RCT was conducted; it was small and the methodology contained some flaws.
 - Observations and results reported were short term; it is hard to tell with this length of follow-up what the longer-term effects are or if there is potential for harm.

Item 10

On February 22, 2015, the Myriad Laboratories provided the Department with a list of suggested additions to coverage. The proposal may be found, in-full, at the following link:

<https://www.colorado.gov/pacific/sites/default/files/Benefits%20Collaborative%20Genetic%20Testing%20Feedback%20Myriad%20Genetics%20February%2012%2C%202015.pdf>

- The Department has carefully considered the feedback therein and responses to each item are provided below.

Hereditary Cancer Syndromes Coverage Recommendations

- Lynch syndrome
 - The Department has decided to expand genetic testing coverage as it pertains to Lynch syndrome as described in Item 6 above.
- Adenomatous Polyposis Syndromes



- The Department *will not* cover testing for the purpose of identifying Adenomatous Polyposis Coli (APC) or MUTYH (mutY Homolog (E. coli)) gene mutations at this time but will revisit this decision in a year's time, as more evidence of clinical utility becomes available.
- 2Next Generation Sequencing (NGS) for Hereditary Cancer Syndromes - More research needs to be done in order to determine the overall effectiveness of such testing, particularly as it pertains to clinical utility. Some of the conditions that have informed the Department decision *not* to cover NGS at this time, are as follows:
 - The potential for finding incidental defects and defects which are not clinically actionable is high.
 - No reliable cost-effectiveness research has been performed in this area.
- **BRCA1 and BRCA2 Testing**
 - In addition to covering BRCA testing under the conditions already specified within CDC Tier 1, the Department *will* cover BRCA1/BRCA2 testing as a companion to Poly-ADP ribose polymerase (PARP) inhibitor treatment, as PARP inhibitors should not be given to women with ovarian cancer who do not have a BRCA mutation.

Prognostic Markers and Disease Activity Coverage Recommendations: Prolaris and Vectra DA

- At this time, the Department *will not* cover Prolaris testing to measure prostate cancer aggressiveness and mortality, nor Vectra DA testing to measure cytokine that are associated with inflammation and damage from arthritis; the evidence currently does not warrant the risks. The Department will, however, review all policy decisions annually and may amend the Genetic Testing Benefit Coverage Standard to include Prolaris and/or Vectra DA at a later date, as more evidence becomes available. Some of the factors that have informed the Department decision *not* to cover testing at this time, are as follows:
 - The tests are rarely used.
 - The tests are expensive and opportunity exists for billing abuse.
 - Evidence of clinical utility currently is insufficient.
 - A lack of evidence for changed treatments and improved outcomes.



Item 11

In August of 2015, the Department received several requests to cover the myRisk Hereditary Cancer Test. All requests can be viewed at the following links:

<https://www.colorado.gov/pacific/sites/default/files/Benefits%20Collaborative%20Genetic%20Testing%20%20Feedback%20Consolidated%20Email%20%282%29%20February%2012%2C%202015.pdf>

<https://www.colorado.gov/pacific/sites/default/files/Letter%20from%20Clinical%20Cancer%20Genetic%20Counselors%20In%20Colorado%20February%2012%2C%202015.pdfh>

- The Department has reviewed the myRisk panel and has determined that, at present, as a whole, it does not meet medical necessity criteria. The Department does cover the tests in the myRisk panel for which there is the most evidence that results impact clinical decision making. However, myRisk also tests for many mutations/conditions which the Department does not cover under the proposed policy because there is insufficient evidence of the tests' ability to impact clinical decision making. As a general principle, the Department does not presently cover multigene panels, and the Department has determined that there is insufficient evidence to make an exception for myRisk.

Item 12

In addition to requesting consideration of myRisk (see item 11 above), sixteen Colorado clinical cancer genetic counselors also offered the following recommendations, which can be found in-full at the link below.

<https://www.colorado.gov/pacific/sites/default/files/Letter%20from%20Clinical%20Cancer%20Genetic%20Counselors%20In%20Colorado%20February%2012%2C%202015.pdfh>

Expanding Lynch syndrome coverage to include "endometrial cancer under age 50" and "synchronous or metachronous colorectal or other Lynch syndrome-related tumors, at any age"

- The Department has determined not to expand the criteria for Lynch syndrome testing, at this time, beyond the criteria previously listed (see Item 6 above).



Ability to appeal a coverage denial for cancer germline genetic testing based on the ordering health care provider's clinical judgment of medical necessity and for situations in which NCCN guidelines are not available

- A provider may request a Reconsideration if a prior authorization request (PAR) is denied; a second clinical reviewer will then evaluate the PAR. Clients may appeal a decision if a service is not authorized upon reconsideration.

Item 13

In August of 2015, the Department received another request to cover the Prolaris Assay from E. David Crawford, MD, Professor of Surgery/Urology/Radiation Oncology, University of Colorado, Denver, which included a link to *An Evaluation of the Economic Impact of CCP Assay in Localized Prostate Cancer*.

- The Department reviewed the information provided and will not cover Prolaris at this time, for the reasons mentioned previously (see Item 10 above).

Item 14

Has the Department added any additional genetic tests to the list of proposed covered services since the last draft of the Genetic Testing Benefit Coverage Standard was shared on July 19, 2015?

- The Department has added several pharmacogenomic tests to the list of covered services in the Genetic Testing Benefit Coverage Standard, the results of which are presently required by Colorado Medicaid prior to approval of certain covered drugs (under the pharmacy benefit). The omission of these tests in previous drafts was an oversight. New additions include the following:
 - CYP2D6 extensive, intermediate, or poor metabolizer
 - G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R, R117H mutations
 - F508del homozygous mutation
 - LDLR DNA Sequence
 - Analysis or LDLR Deletion/Duplication Analysis for large gene rearrangement testing, under the following conditions:
 - For Homozygous familial hypercholesterolemia and Kynamro appropriateness.
 - LDLR Deletion/Duplication Analysis is covered only when Sequence Analysis is negative.
 - APOB and dPCSK9 testing
 - If both the LDLR DNA Sequence and LDLR Deletion/Duplication analysis tests are negative, but a strong clinical picture exists.



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- Immunodeficiency disorders: Common Variable Immunodeficiency (CVID); Severe Combined Immunodeficiency (SCID); X-Linked Agammaglobulinemia; X-Linked with Hyperimmunoglobulin M (IgM) Immunodeficiency; Wiskott-Aldrich Syndrome
- Urea cycle disorder (UCD)
- To view further details regarding when the above tests are covered, refer to the most recent version of the Genetic Testing Benefit Coverage Standard posted at the following link:

<https://www.colorado.gov/pacific/sites/default/files/Benefits%20Collaborative%20Genetic%20Testing%20Revised%20Draft%20Standard%20%E2%80%93%20September%202015%20February%2012%2C%202015.pdf>